

### **REMARKS**

Applicant respectfully requests reconsideration. Claims 1, 2, 115-122, 124, 130-156 and 161-169 were previously pending in this application. Claims 1, 115, 130, 137, 147 and 162 are amended. New claims 170-177 are added. Support for these amendments and new claims can be found in the specification at least on page 11 lines 15-16, page 12 lines 12-14, page 13 lines 3-9, page 16 lines 31-33, page 30 lines 19-20, page 31 lines 28-29, page 32 lines 1-2, page 63 lines 22-24, page 68 lines 17-18, page 70 lines 30-31, and page 73 lines 6-12, and in claims 115, 130, 137 and 147. As a result, claims 1, 2, 115-122, 124, 130-156 and 161-173 are pending for examination with claims 1, 115, 130, 137, 147, 162 and 170-177 being independent claims. No new matter has been added.

No additional claims fees are considered due in view of the additional claims fees paid previously.

#### ***Rejection under 35 U.S.C. §112***

Claims 1, 2, 115-122, 124, 130-156 and 161-169 are rejected under 35 U.S.C. §112 for allegedly lacking enablement.

The Examiner considers that the specification does not enable “*labeling* of individual units in a polymer for determining the identity of each individual unit sequentially via linear analysis through a nanochannel” (emphasis added) particularly with respect to polymers that are not nucleic acids or proteins. The Examiner has previously acknowledged that the specification is enabling for the *identification* of individual units of a polymer but not the *labeling* of each individual unit. The Examiner maintains the rejection based primarily on (a) the breadth of the term “polymer”, (b) the level of experimentation required to overcome steric hindrance relating to extrinsic labeling of every unit within a polymer, and (c) the level of experimentation required for intrinsic labeling of every unit within a polymer. Applicant has previously provided a full Wands analysis relating to the claimed invention. For brevity, Applicant here addresses the specific issues raised by the Examiner.

Regarding the term “polymer”, without conceding the correctness of the rejection, and rather in the interest of expediting prosecution, Applicant has amended claims 1, 115, 130, 137, 147 and 162 to recite that the polymer is a nucleic acid or a polypeptide. Support for this amendment can be

found in the specification at least on page 31 lines 28-29 and page 32 lines 1-2. Dependent claims 2, 116-122, 124, 131-136, 138-146, 148-156, 161, and 163-169 depend from the above-mentioned amended claims. New claims 170-177 also contain the limitation that the polymer is a nucleic acid or a polypeptide.

Regarding the issue of extrinsic labeling of polymers, the Examiner asserts that a high degree of experimentation would be necessary “in order to incorporate a light emissive compound for each unit of the polymer.” Without conceding the correctness of the rejection, and rather in the interest of expediting prosecution, Applicant has amended claims 1, 115, 130, 137, 147 and 162 to recite, in part, that signals or polymer dependent impulses are detected from less than all linked units in a polymer. Similarly, new claims 170-173 recite that signals or polymer dependent impulses are detected from unit specific markers bound to less than all linked units in a polymer. Support for these amendments and new claims can be found in the specification as recited above. Accordingly the claims no longer require that all units be detected, and nor that all units be labeled. The issue of steric hindrance when “all four bases in the DNA (are) tagged by different fluorophores”, as posed by the Examiner, is therefore moot since the claimed methods can be performed with less than all units being labeled. The teachings of Sauer et al. (J. Biotechnology 2001, 86, p181-201) relating to the labeling of nucleotides are similarly moot.

Notwithstanding the above, and rather for the record, Applicant notes that the Examiner acknowledges that the specification teaches that “some of the nucleotides may be intrinsically labeled to reduce steric hindrance” and that it provides guidance relating to the use of extrinsic “labels that are small and neutral in charge to reduce steric hindrance”. Thus, contrary to the Examiner’s conclusion, the specification does indeed provide guidance relating to extrinsic and intrinsic labeling of all units within a polymer.

Regarding the issue of intrinsic labeling of polymers, the Examiner states that “the specification does not clearly define the practice of identifying the specific units through intrinsic label(s) that distinguish individual units of a polymer, without using ion conductance measurements”. However, in the same passage, the Examiner acknowledges that the specification teaches that the four native nucleotides have distinct absorption maxima. Thus clearly the specification does provide a non-ion conductance measurement through which individual units of a

nucleic acid can be distinguished. The Examiner further acknowledges that a high degree of experimentation *would not be necessary* to identify intrinsic labels for individual units of nucleic acids. However the Examiner further states that “there is no corresponding intrinsic property of amino acids provided which would serve as an ‘intrinsic’ label for the practice of the invention”. Applicant respectfully disagrees. First, the specification teaches at least on page 33 line 29 through to page 34 line 1 that the shape of a unit provides information about its identity. Moreover at least some amino acids can be distinguished based on their absorption maxima similarly to nucleotides (e.g., tryptophan, tyrosine and phenylalanine absorb at 280, 274 and 257 nm respectively). Second, the claimed methods do not require intrinsic labeling of amino acids and nor do they require labeling of all amino acids. Applicant maintains that based on the knowledge in the art and the guidance provided by the specification that one of ordinary skill in the art would be able to analyze polypeptides using intrinsic and/or extrinsic labels.

The Examiner further challenges the claims on the basis that “Applicant has given no indication that such an apparatus or device, comprising nanochannels or a nanoplate has been reduced to practice”, and cites *In re Ghiron* 442 F.2d 985, 991, 169 USPQ 723, 727 9CCPA 1971) in support. Respectfully, the specification provides enabling guidance relating to apparatuses that can be used for the claimed methods, as evidenced by the US 6355420 claims 33-48.

The Examiner cites Chan (Mutation Research, 2005, 573, p13-40) and Rhee et al. (Trends Biotechnology, 2006, 24, p580-586) for a number of propositions relating to nanopore sequencing. Nanopore sequencing is a sequencing method that relies on nucleotide-specific ion conductance measurements. The claimed methods explicitly exclude such measurements, and therefore these teachings are moot. The Examiner further cites Braslavsky et al. (Proc Natl Acad Sci USA, 2003, 100, p3690-3694) for teachings relating to background fluorescence and impurities. One of the references that is cited by Braslavsky et al. for this teaching is Sauer et al. discussed above. The claimed methods do not detect signal from every unit and thus do not require that every unit be labeled. The claimed methods are therefore different from those of Sauer et al. and Braslavsky et al., and the teachings relied on by the Examiner are therefore moot.

In view of the foregoing, Applicant maintains that undue experimentation is not required for one of ordinary skill in the art to practice the claimed invention.

Reconsideration and withdrawal of the rejection is respectfully requested.

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: February 25, 2008

Respectfully submitted,

By 

Maria A. Trevisan, Reg. No. 48,207  
WOLF, GREENFIELD & SACKS, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
(617) 646-8000